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CLINICAL PROCEEDINGS

OF THE CHILDRENS HOSPITAL

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CARDIAC FAILURE IN CHILDREN

Special Report No. 263

John O. Nestor, M.D.

The diagnosis of cardiac failure in older children is ordinarily not more difficult than in adults; however, it sometimes becomes a perplexing problem in small infants where it is often difficult or impossible to differentiate cardiac failure from acute pulmonary infection with peripheral vascular collapse.

Since the liver is normally palpable throughout childhood, and in small infants is frequently felt extending two or three centimeters below the right costal margin, it is sometimes difficult to decide whether such a palpable liver is due to the congestion resulting from cardiac failure or not. It is true that in failure the liver is usually firm, has a sharp edge, and may even be tender; normally the liver is quite soft and without a definite edge.

The venous pressure, which is of great value in adults, is of little diagnostic aid in infants because it is technically a difficult procedure to perform in a small, desperately ill child, and normal values have not been established. Above the age of four years the normal values approximate those of adults and range from 40 to 120 mm. of water or saline.

Roentgenographic examination may be of great value in making a differential diagnosis for, if the heart is not enlarged, cardiac failure is probably not present. Roentgenograms may be misleading in determining cardiac enlargement of infants and should the heart appear to be large when the film is examined, the fluoroscope should be employed to confirm the heart size. It is not unusual to find that a heart which appears grossly enlarged on roentgenogram will prove to be within normal limits in size and configuration when viewed under a fluoroscope.

It is particularly important to be able to make this difficult differential diagnosis for two reasons. If the child is in cardiac failure, he should be digitalized, whereas if he is in peripheral collapse, digitalis may actually be harmful, for it is common knowledge that the cardiac output is diminished about 10 per cent by digitalization of the normal heart. If this happens in a desperately ill child whose cardiac output is already inadequate, the possibilities are obvious. Then, too, many small infants go into cardiac failure because of certain congenital defects of the heart and great vessels, which are surgically correctable, chief among which are coarctation of the aorta, patent ductus arteriosus, tetralogy of Fallot, and pure pulmonary stenosis.

Once it is decided that cardiac failure exists, an attempt should be made to determine whether it is predominantly left-sided (forward failure) or right-sided (backward failure), for we see examples of each in children just as we do in adults. Predominantly left-sided failure is characterized primarily by pulmonary engorgement, and therefore dyspnea, tachypnea, grunting, and cough are prominent signs and symptoms, whereas in predominantly right-sided failure, congestion of the liver, and peripheral edema are prominent.

Some of the causes of left-sided failure in children are:

1. Acute glomerulonephritis
2. Paroxysmal auricular tachycardia
3. Endocardial fibroelastosis
4. Patent ductus arteriosius
5. Coarctation of the aorta
6. Aortic and sub-aortic stenosis
7. Anomalous left coronary artery arising from the pulmonary artery
8. Coronary insufficiency due to arteriosclerotic heart disease
9. Tumor of the left auricle or ventricle

The causes of right-sided or backward failure are:

1. Active rheumatic heart disease
2. Most forms of congenital heart disease
3. Tumors of the right side of the heart
4. Pulmonary heart disease (cor pulmonale)
5. Constrictive pericarditis

Once cardiac failure has been diagnosed the principles of treatment are the same as for adults, but there are some variations in emphasis, methods, and dosage. To get a patient to rest is usually not the difficult problem it frequently is in adults, because most small children in failure are much too sick to try or to want to move much. Occasionally, an older child in failure from active rheumatic fever may attempt too much activity and need to be restrained or sedated. The diet should be low in calories and salt, and high in vitamin content. One need not restrict fluids for this is not a problem. In fact, one should make a special effort to see that these patients obtain an adequate fluid intake rather than permit them to become dehydrated, as is frequently the case.

It is well to standardize technique with a specific group of drugs with which one is familiar. The following routine has been found quite satisfactory:

1. *Digitalis:* For oral use the tincture of digitalis is satisfactory. It contains 100 mg. per ml. and should be measured accurately in a small syringe rather than from a dropper, for 1 ml. may contain from 20 to 60 drops depending on the size of the dropper and the angle at

which it is held. The digitalizing dose is calculated on the basis of 30 mg. per kg. of body weight, and the daily maintenance dose is usually about one-tenth of this digitalizing dose. On rare occasions the same dose of the tincture may be given rectally in 50 or 100 ml. of water. Occasionally, in a desperately ill child who cannot take oral medication, and if it is impossible to get a needle into a vein, one may use digitoxin intramuscularly in a dose of 0.1 mg. per 10 lb. of body weight. Cedilanid (Lanatoside C) is very effective for rapid digitalization when given intravenously in the same dose—0.1 mg. per 10 lb. of body weight. If digitalization is to be maintained for a few days by the use of parenteral cedilanid, the full digitalizing dose should be given daily divided into four doses given every six hours until it is practical to go over to a maintenance dose of tincture of digitalis when the condition of the child has improved.

Children tolerate digitalis well, and it seems to be a fairly safe drug; for the therapeutic dose is only 35 to 40 per cent of the toxic dose. In fact, it is generally recognized that in treating paroxysmal auricular tachycardia with digitalis, it is usually necessary to give two to three times the usual digitalizing dose to produce the desired reversion to a normal rhythm. It is also interesting to note that one does not ordinarily digitalize a child in cardiac failure due to active rheumatic fever, but does not hesitate to digitalize a child in failure due to acute nephritis.

2. *Morphine:* is of particular value in cases of cyanotic congenital heart disease when the patient is having a spell of unconsciousness due to anoxia or is having a bout of paroxysmal dyspnea. The dose is not more than 1 mg. per 5 kg., or 11 lbs., and the result of therapy in such cases is sometimes both spectacular and gratifying.
3. *Quinidine:* is occasionally used to treat paroxysmal auricular tachycardia when digitalization has failed after two or three times the usual digitalizing dose has been given. The dose is calculated on the basis of 3 mg. per lb. of body weight and is given every three hours until the tachycardia has ceased or toxic symptoms have appeared. A small test dose is always given first to eliminate the possibility of a severe reaction to the usual dose.
4. *Diuretics:* members of the xanthine group such as theocalcin are frequently of value when used in doses of 5 to 15 grains three or four times a day, depending on the size of the child. Occasionally aminophylline and a barbiturate given as a suppository may be of benefit. Mercurial diuretics are of considerable value in children, and one may use any of those commonly used in adults; however, thiomerin is much safer because it does not produce a slough if it infiltrates the

subcutaneous tissues, and it is as effective as the other mercurial diuretics. The usual dose is anywhere from 0.25 to 1 cc. depending on the size of the child. Ordinarily one does not use a mercurial diuretic in cardiac failure due to acute nephritis but frequently uses it in failure due to acute rheumatic fever.

The physical means of treating cardiac failure in infants are important and consist chiefly of:

Bed rest,

Oxygen,

Phlebotomy in which it is necessary to remove relatively large amounts of blood rapidly in order to obtain the desired effect, and

Tourniquets applied to three of the extremities and rotated every 15 or 20 minutes leaving a different extremity free each time. A convenient method is to use three sphygmomanometer bands at a pressure of 40 or 50 mm. of Hg.

Not infrequently small infants will go into acute cardiac failure because of a surgically correctable congenital defect of the heart and, if the diagnosis can be made, surgery may be life-saving even though the risk is great. The following are the usual anomalies and the operations recommended to correct them:

1. Ligation of a patent ductus arteriosus,
2. Excision of a coarctation of the aorta with anastomosis,
3. Pott's or Blalock-Taussig anastomosis for tetralogy of Fallot,
4. A valvulotomy for a pure or valvular pulmonary stenosis.

SUMMARY

The diagnosis and treatment of cardiac failure in children has been briefly outlined, emphasizing (1) the difficulty of diagnosis in infants, (2) a routine method of treatment with a specific group of drugs and a standardized technique, and (3) the surgical treatment of cardiac failure resulting from congenital abnormalities of the heart and great vessels.

THE SORE THROAT AND INTRAORAL MEDICATION

EDITORIAL

Stanley Wolf, M.D.

Prior to the advent of the sulfonamides the treatment of pharyngitis consisted primarily of warm gargles or of painting a liquid preparation, usually some type of dye, on the posterior pharynx. Instead of eliminating the use of gargles and paints, antibiotics have complicated the treatment.

Almost daily one notes the appearance of a new proprietary preparation designed to modify or cure this common affliction. Since the number of sensitizations resulting from use of these preparations is increasing, perhaps closer evaluation is indicated.

Gargles: Ten practicing pediatricians were polled for their opinions about the efficacy of gargles. All agreed that use of special medications in the gargle was unnecessary. The use of saline gargles, perhaps, with added $NaHCO_3$, was considered to be of some value in alleviating symptoms. It was also agreed that many mothers appreciated being able to help in the therapeutic regimen. Several physicians felt that the returns to be expected from routine use of gargles in many cases did not justify the expenditure of time and energy. Obviously then, the use of gargles depends on individual preference.

Troches: Troches are now available containing almost any desired antibiotic or group of antibiotics in combination with a local anesthetic. These are available in any desired flavor or color. Since sensitization frequently arises from prolonged local contact with an antibiotic, the local use of any systemically used antibiotic is definitely contraindicated. Some antibiotics such as bacitracin or tyrothricin may be used locally if one feels the risk of an allergic reaction is justified. Reaction to the "caine" group of anesthetic agents is also not uncommon. Such reactions may take many forms. In fact, the symptoms of pharyngitis may persist as a result of use of these drugs.

Dyes: Drugs such as merthiolate and gentian violet are now seldom used to paint the throat since their palliative effect is so transient.

In summary, it is important to reconsider the value of intraoral medications. Since parenteral medications are so often used successfully in these cases, it is probably best to avoid intraoral use of any possible sensitizing agent whenever possible. Saline gargles remain a matter of individual preference. Painting the throat is seldom, if ever, indicated.

NEWS NOTE

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LYMPHOSARCOMA OF THE TONSIL

Case Report No. 264

Joseph P. Giardino, M.D.
David F. Bell, Jr., M.D.

INTRODUCTION

In the course of numerous routine tonsillectomies performed on children, lymphosarcoma of the tonsil is very infrequently discovered. The case reported herein presented the clinical findings of respiratory obstruction due to enlarged tonsils and adenoids. An emergency tonsillectomy and adenoidectomy were done. The tissue specimen was examined microscopically and revealed primary lymphosarcoma of the tonsils.

Treatment consisted of postoperative irradiation and the administration of triethylene melamine as maintenance therapy.

CASE REPORT

This six-year-old colored female was admitted to The Children's Hospital on October 14, 1952 because of difficulty in breathing for two days. The child was apparently in good health until four days prior to admission when she developed a sore throat for which aspirin and gargling offered no relief.

Two days later she was seen in the Out-Patient Department with inflamed, enlarged tonsils, enlarged cervical nodes, moderate injection of the eardrums, and fever. There was moderate respiratory difficulty due to enlarged tonsils and adenoids. The child was given penicillin intramuscularly and symptomatic treatment consisting of aspirin, fluids, nose drops, and local heat to the cervical nodes. Over the next two days her respirations became more noisy and labored and she was admitted to the hospital on October 14, 1952. Tuberculosis contact was denied. All immunizations had been previously received. Family history, past history, and review of systems were non-contributory.

Physical examination on admission revealed a well-developed, well-nourished colored female who appeared acutely ill and in respiratory distress—having noisy, grunting respirations, indicative of obstruction and some cyanosis of the lips. She was alert and fairly cooperative. The pertinent findings were: temperature 101.8 F., pulse 120 per minute, labored respirations 35 per minute, and blood pressure 100/60.

The mucous membranes of the mouth were very dry. The pharynx and uvula were injected moderately and had several soft whitish patches on them. The tonsils were markedly enlarged, red, covered by exudate, and encroached on the base of the tongue so as to allow only a minimal airway. There was some resistance to flexion of the neck due to marked bilaterally enlarged, tender, firm, hot, cervical nodes. Numerous submaxillary and submental enlarged tender nodes were noted. These were found to be discrete and firm. The abdomen was soft and non-tender. The liver edge and splenic tip were palpable. Right costovertebral angle tenderness was present. Examination of the skin disclosed fair turgor; no rashes were noted. The clinical impression was:

1. Acute tonsillopharyngitis, adenoiditis with obstructive respirations,
2. Cervical adenitis,

3. Bilateral ototis media, acute catarrhal, and
4. Possible pyelonephritis.

Laboratory workup on admission included a complete blood count which revealed 11.0 grams of hemoglobin; 38 per cent microhematocrit; and 23,700 white blood cells with 45 segmented cells, 13 band forms, 2 young forms, and 40 lymphocytes per 100 cells. Platelets were normal; there was slight hypochromia of the red blood cells. Admission urinalysis was reported as clear and acid. Specific gravity was 1.015; albumin, 30 milligrams per 100 milliliters; red blood cells, 1–3; and white blood cells, 3–6. Urine culture disclosed no growth. Sugar and acetone were negative. On throat culture, no *Corynebacterium diphtheriae* were seen. There was normal flora with *Beta hemolytic streptococci*. A PPD #1, done on October 16, was reported as negative.

Roentgenograms of the chest showing the neck in the postero-anterior and lateral views were taken. These revealed the left border of the heart to be somewhat straight although the heart itself was within normal limits. Nevertheless, a cardiac investigation was felt to be in order. The cervical spine and retropharyngeal region revealed no pathology. The pulmonary parenchyma appeared normal.

On admission, the child was placed in an oxygen tent and was given parenteral fluids. Aureomycin and penicillin were administered, but she continued to run a septic temperature. To relieve the respiratory embarrassment, a nasal catheter was passed to obtain an adequate airway, but despite therapy the child was tiring and near exhaustion. She was seen by Drs. A. Walker and M. Fisher of the Ear, Nose and Throat Department, who recommended a tonsillectomy and adenoidectomy which were performed on October 17, 1952. A specimen of tonsillar and adenoid tissue was sent to pathology for microscopic examination. The postoperative course was uneventful and the child's condition was markedly improved.

The microscopic examination of the specimen was reported on October 20, 1952 as lymphosarcoma of the tonsils, primary. The microscopic description was as follows:

Sections of the tonsillar tissue showed squamous epithelium partially covering neoplastic lymphoid tissue. The normal architecture of the tonsil was completely replaced by cells that were relatively uniform in size and were composed of round or oval dark-staining nuclei and a minimal amount of eosinophilic cytoplasm. Only a few mitotic figures were seen.

The supporting fibrous stroma was scanty and there was an increased number of blood vessels. Some areas of the tonsil showed acute necrosis. The fibrous septa were infiltrated by neoplastic cells.

On October 20, 1952, the child was presented to the Tumor Board and it was recommended that she have a bone marrow examination and irradiation to the oropharynx, followed by the administration of triethylene melamine as maintenance therapy. The bone marrow examination was essentially normal.

From October 22, 1952 to November 4, 1952, each side of the hypopharynx and lateral cervical and submental areas were irradiated with single doses of 162 roentgens eight times for a total of 2592 roentgens. The cervical, submaxillary, and submental nodes were diminished in size. Triethylene melamine, 1 milligram daily, was then started on October 31, 1952 and continued until the child's discharge on November 6, 1952. During this period, daily peripheral leukocyte and differential counts were obtained ranging between 4,500 and 6,500 with relatively normal differential counts. Repeated urinalyses were negative. The child was discharged on triethylene melamine therapy 1 milligram every other day to be followed in the Tumor Clinic. There were no signs of toxic manifestations of the drug.

During her weekly clinic visits she has had repeated blood studies including follow-up bone marrow examinations. The hematologic picture on the whole has remained relatively normal with the exception of 10 to 20 per cent eosinophilia. The bone marrow examination revealed an increase in the lymphocytes with some abnormal forms and a slight increase in the eosinophils. Clinically, the lymph nodes in the cervical, submental, submaxillary, axillary, and inguinal areas have remained unchanged. Only on one occasion was the liver edge palpable. No side-effects have been manifested by the dosage of triethylene melamine. As of this date, February 16, 1953, the child has returned to school and shows no signs of regression.

DISCUSSION

According to Sugarbaker and Craver[1] lymphosarcoma is a malignant, neoplastic disease of lymphoid tissue capable of arising in any lymphoid aggregate. It may run an acute or chronic course and is almost always highly radiosensitive. Death is the usual outcome with many clinically unsuspected metastases. The biologic forces inciting lymphoid tissue to malignant growth are unknown but are believed to be similar to those activating other tissues.

In their study[1] a marked frequency of chronic infection was noted, especially of the upper respiratory tract in patients in whom the first appearance of lymphosarcoma occurred as a nodal swelling in the neck. In these patients, approximately 32 per cent complained of some chronic infection of the upper respiratory tract. It was brought out that the role of tuberculosis is much less evident in lymphosarcoma than it is in Hodgkin's disease. Theoretically, it is possible that prolonged stimulation of lymph nodes may eventuate in malignant growth.

Unlike carcinoma, where involvement of a chain of lymph nodes is progressive and secondary, lymphosarcoma develops in the lymphatic system. It seems to spread, involving either a whole chain of nodes simultaneously or widely separated node groups. This favors a theory that, perhaps, a readily diffusible activating agent is responsible for extension. The fact that tumor nodules are found in organs not ordinarily containing lymphoid tissues, and that patients may remain cured following surgical removal of involved nodes, suggests that cell emboli alone are responsible. Ewing believes that extension probably involves both dissemination of an exciting agent and cell embolism.

The incidence of lymphosarcoma seems higher in males than in females in a ratio of a little more than 2:1. Lymphosarcoma is uncommon before the age of 20 years, and in comparison with other types of cancer, is not a common disease.

Because this disease has innumerable possible primary sites and, since secondary extension becomes so widespread, enumerating clinical signs and symptoms would become too involved, it should be emphasized that the differential diagnosis of lymphosarcoma and other lymphomas and related

diseases should be attempted only after microscopic examination of a biopsy specimen. However, some investigators (Sugarbaker and Craver[1]) found that in 65 per cent of the patients with lymphosarcoma, the initial sign was visible and palpable external nodal swelling which was painless in almost all cases. The nodes involved were, as a rule, a whole chain, but occasionaliy a solitary, enlarged node might be present.

Abdominal symptoms occurred first in 17.5 per cent of cases; and in 11.6 per cent, difficulties of the upper respiratory tract were the first complaint; e.g., sore-throat, tonsillar swelling, nasal obstruction and bleeding. Thoracic and bone symptoms constituted the rest. Constitutional symptoms occurred late in the disease. As for the primary site, they[1] found that of the 34.5 per cent extranodal foci, the tonsils constituted the highest percentage, or 14. These observers noted that the following organs were most frequently affected by secondary metastases:

1. Spleen—21 per cent
2. Lungs—12 per cent
3. Bones—9.7 per cent
4. Liver—8 per cent
5. Skin—5 per cent

In 1948 Sorin[2] reported on the clinical and therapeutic study of lymphosarcoma of the tonsils, having accumulated 104 cases over a period of 20 years at the Curie Foundation. Like most investigators, he believes the treatment of choice is radiation therapy. Seventy-nine of his cases were treated with radiotherapy and 29 patients recovered. Poor results occurred with other modalities of treatment. Those patients with distant metastases numbered 52, only 2 of these surviving for a period of 5 years.

Sugarbaker and Craver[1] treated 108 of 146 patients with lymphosarcoma with some method of irradiation, 13.9 per cent of whom survived 5 years or more. Most of the surgically treated patients were given immediate local external irradiation prophylactically and 24 per cent of these had a survival period of 5 years or more. These investigators believe the best single dose of roentgens was from 400 to 600 with a total of 2,000 to 3,000 per field. They also recommend that surgical extirpation made in localized lymphosarcoma should be attempted more frequently.

According to Orthon[3] surgery is limited to small tumors with or without slight lymph node involvement, utilizing a combined operation of dissection of the neck, with complete removal of the tonsil and surrounding tissue either by cold knife or cautery. The prognosis, however, is not good. On the other hand Lampe[4] believes tonsillectomy is useless; and, that except for uncommon types of tumors of salivary-gland origin, the malignant tumors which arise in the tonsils are solely a radiotherapeutic problem.

He believes that at the present time, the survival rate for skillful radiotherapy of the tonsillar malignancies is 30 per cent for a five-year period. If tonsillar malignancies were less frequently confused with inflammatory processes and less time were consumed in chemotherapy, survival rates would undoubtedly be higher.

Another agent used in treatment of lymphosarcoma, and which we have employed as an adjunct in our case is triethylene melamine. However, it has been pointed out that the use of this drug should not be undertaken without certain prerequisites and precautions[8]. It has also been brought out that the acid pH of the stomach increases the stability and decreases the absorption of triethylene melamine, and that avidity for organic molecules binds it firmly to food. Thus the drug should be given to a fasting patient. In the treatment[8] of 38 adults with neoplasm, five of whom had lymphosarcoma, the regimen generally consisted of:

1. Oral administration of 5–10 milligrams of triethylene melamine in single doses before breakfast, food having been withheld for at least one hour.
2. In most cases, dose was repeated the next day, the amount depending upon the nature and stage of the disease and the patient's response to previous treatment.
3. White blood-cell counts at 3-day intervals until a leukopenic response was noted or for 1–2 weeks when additional triethylene melamine might be administered.
4. Platelets, hemoglobin, and blood urea-nitrogen were observed.
5. Treatment was continued until remission was effected or signs of toxicity occurred. If a leukopenic response occurred after 3–4 weeks without collateral evidence of clinical improvement, further treatment was considered ineffective. The toxic effects encountered by several authors (8, 9) in the use of triethylene melamine were:
   A. Anorexia, nausea, vomiting (believed to be due to action of the drug and not to local irritation),
   B. Leukopenia,
   C. Anemia,
   D. Thrombocytopenia with or without purpura,
   E. Bone marrow aplasia,
   F. Renal damage (found in all patients who died in their series)[8].

Triethylene melamine may be beneficial in the treatment of diseases which involve tissues in widespread anatomic areas. Because of its oral effectiveness it can be given over a prolonged period of time. Its relative freedom from side reactions, as contrasted to nitrogen mustard, makes it desirable also.

It has been reported[9] that triethylene melamine has a transitory effect

and has been recommended that the drug be given in maintenance doses at intervals no greater than 1–2 weeks because most patients demonstrated continued evidence of disease activity. Poor results have been obtained in the patients with rapidly extending or recurring disease and in those patients with tumors causing local tissue invasion.

SUMMARY

A case of lymphosarcoma of the tonsils is presented and a treatment plan with irradiation and triethylene melamine as maintenance therapy is outlined. Lymphosarcoma has been briefly discussed.

REFERENCES

1. Sugarbaker, E. D. and Craver, L. F.: Lymphosarcoma: A Study of 196 Cases with Biopsy,
2. Sorin, A.: Clinical and Therapeutic Study of Lymphosarcoma of the Tonsil, Bull. Assoc. france, f. L'etude du cancer **35:** 65–85, 1948.
3. Orthon, H. B.: Malignant Neoplasms of the Tongue, Tonsil and Hypopharynx: Evaluation of Surgical Treatment, Am. Acad. Ophth. and Otolar., pp. 226–30, January 1951.
4. Lampe, I.: Malignant Neoplasms of the Tongue, Tonsil and Hypopharynx: Evaluation of Radiation Therapy, Am. Acad. Ophth. and Otolar. pp. 231–36 January 1951.
5. Kearny, J.: Medical Annals of the D. of C. **21:** 3, 379–83 (July) 1952.
6. Whitcomb, C. A.: Sarcoma of the Tonsil: Impressions Made by Seven Cases, Arch. Otolar. **38:** 1–9, 1943.
7. Bernen, E. G. E.: Radiation Therapy of Malignant Tumors of the Tonsil, *in Treatment of Cancer*, Pack and Livingston, New York, 1940.
8. Bayard, E. D.; Stickney, J. M.; Hall, B. E., and Watkins, C. H.: Cervical Observations in the Use of Triethylene melamine, J. Am. Cancer Soc. **5:** 2, 336–343 (March) 1952.
9. Rundles, R. W. and Burton, W. B.: Triethylene Melamine in the Treatment of Neoplastic Disease, J. Hemat. **7:** 5, 483–507 (May) 1952.
10. Mitchell and Nelson: *Textbook of Pediatrics*, 5th Ed.

HEREDITARY DEFORMING CHONDRODYSPLASIA

Case Report No. 265

Allyn Giffin, M.D.
William S. Anderson, M.D.

Hereditary deforming chondrodysplasia is a rare disease of bone. Ehrenfried[1], in his classical description of the disease has emphasized the three most striking features:

1. The occurrence of multiple more or less symmetrical cartilaginous and osseocartilaginous growths within and upon the skeletal system, generally benign and resulting from a disturbance in the proliferation and ossification of the bone-forming cartilage;
2. The occurrence of certain typical secondary distortions and deformities of the skeleton, and,
3. the demonstration of inheritance in a large proportion of the cases.

A case presenting multiple internal and external chondromas that was

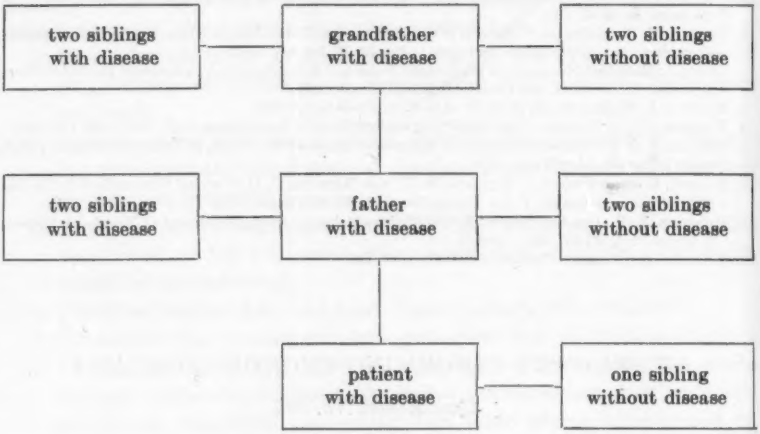
recently seen in Children's Hospital, which satisfies the above description is herein presented.

J. N., a six year old white male, was admitted on March 3, 1953, because of acute laryngo-tracheo-bronchitis of one day's duration.

Past medical history revealed that this child had been a patient in Children's Hospital on two previous occasions: once, at three weeks of age for pyloric stenosis, which was surgically corrected with successful results, and again, at one year of age with bilateral bronchopneumonia, from which he made a complete recovery. He had had no other serious illness or operations.

The patient was born at term, the product of a normal, spontaneous delivery; the birth weight was 4 pounds 15 ounces.

He sat up at 7 months; walked at 14 months; and talked at 20 months. He had always been small for his age, and had never gained weight well. He was in the first



grade, but was not doing well in his school work. He was active and alert in play. Since three years of age the parents noticed that he had had "knots" on his wrists, knees, and along his ribs. These had never caused him any trouble and had been gradual in their growth.

The child had always been a poor eater, but his intake had been adequate and diversified. He had no vitamin supplements until he was four years old.

Family history revealed the mother and a sister of five years to be living and well. Neither had any bone abnormalities. An older brother had died in infancy of pyloric stenosis. The father was a diabetic, and stated that he had "knots" on his knees as long as he could remember. On further inquiry it was found that an aunt and an uncle in one generation, and the grandfather, a grandaunt, and a granduncle in the third generation all had abnormal bony protuberances (see chart). In none of these people did the lesions ever cause symptoms nor so far as is known did they contribute to their death.

Physical examination revealed an undernourished six-year-old boy who appeared

to be the size of a four-year-old. He was in moderate respiratory distress with a "croupy cough" and some retraction of the lower costal cage. He weighed 33 pounds and was 42 inches tall. Temperature was 100.0 F.; pulse, 120 per minute, and respirations, 28 per minute.

Examination of the scalp revealed lesions typical of tenia capitis. There was generalized pharyngeal inflammation with large cryptic tonsils. The anterior cervical lymph nodes were slightly enlarged. The eyes, ears and nose were negative. There was a rapid heart rate, but no enlargement or murmurs were noted on percussion or auscultation. The lungs were resonant throughout on percussion. Breath sounds were clear except for a few rhonchi at the bases. The abdomen was soft; there was no tenderness. The liver and spleen were both palpable 1 centimeter below the costal margin. No other masses were palpable. Examination of the genitalia revealed a

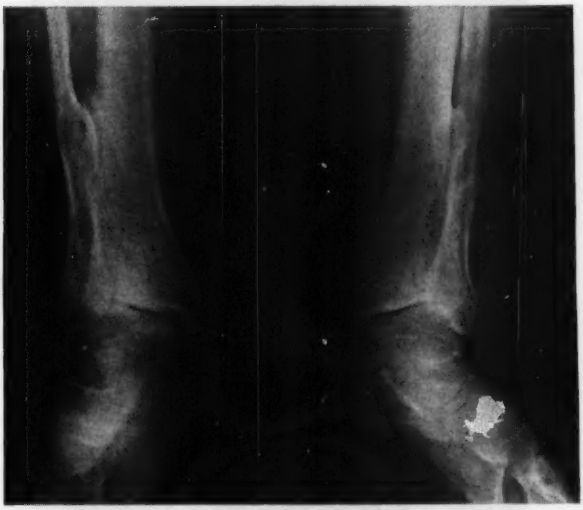


Fig. 1. Roentenogram of the ankles of the patient's father, showing numerous external chondromata.

normal male. Neurological reflexes were physiological. There was poor muscular development throughout. There was a mild thoracic scoliosis. The costochondral junctions of the ribs presented a rosary which was quite sharp on palpation and there was a Harrison's groove on both sides giving the appearance of a mild pigeon chest. There was a widening of the metaphyseal areas with bony protuberances and easily palpable spicules.

Laboratory examinations included a negative urinalysis and a serological test for syphilis which was also negative. Complete blood count revealed 12.1 grams of hemoglobin and a microhematocrit of 33 per cent. There were 14,400 white blood cells with 72 segmented cells, 2 band forms, 2 young forms, 23 lymphocytes, and 1 monocyte per 100 cells. Serum calcium was 9 milligrams per 100 milliliters. Inorganic phosphate was 5.8 milligrams per 100 milliliters and serum alkaline phosphatase was 4.4 Bodansky units. The P.P.D. No. 1 was negative.

X-ray examination of the entire skeletal system showed that only the bones of the face, skull and vertebrae were without abnormal bony and cartilaginous growths. All costochrondral junctions of the ribs showed widening and several had definite internal chondromas. Several areas of decreased calcification were noted in the innominate bones. The metacarpals, the scapulae and the clavicles had small external chondromas. External chondromas were found at the metaphysis of both fibulae, the distal metaphysis of the right fibula, and the distal metaphysis of the right ulna and

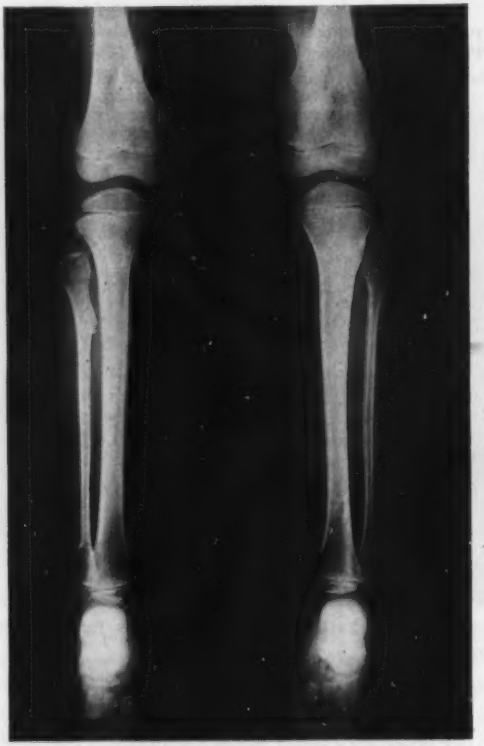


Fig. 2. Lower extremities of the patient, demonstrating both internal and external chondroma.

radius. There was considerable deformity of the distal end of the right ulna and a compensatory bowing of the right radius. The bone age of this boy was considerably retarded: three years, three months, when compared with the plates in Todd's "Atlas."

Skeletal films of the father also revealed numerous external chondromas of the long bones. It is interesting to note that the distal metaphysis of the right ulna of the father presented a deformity similar to that seen in our patient.

X-rays of the long bones of the patient's five-year-old sister revealed no abnormalities and her bone age was five years.

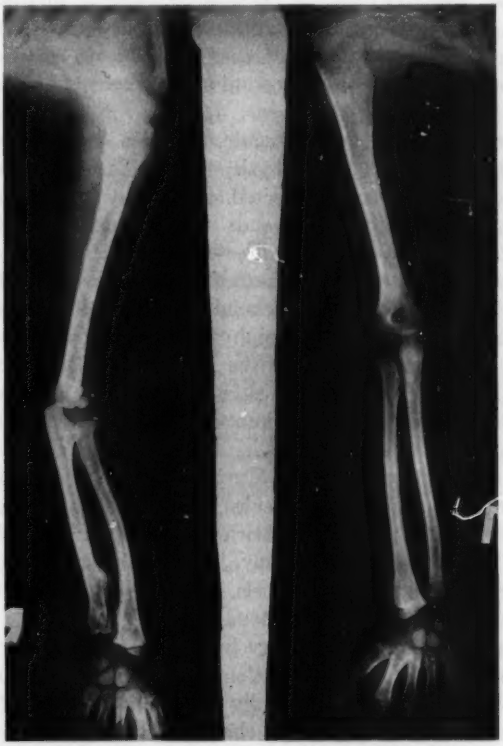


Fig. 3. Upper extremities of the patient, demonstrating both internal and external chondroma. Note also the deformity of the right ulna.

DISCUSSION

This disease has been discussed in the literature under a great variety of titles: multiple exostosis, multiple congenital osteochondromatosis, chondral dysplasia, dyschondroplasia, and many others. We believe that the designation used here—hereditary deforming chondrodysplasia—is a more suitable descriptive term. Also, internal and external chondroma are the best names to describe the individual lesions of the disease.

There is not complete agreement as to the histogenesis of chondrodysplasia. It is Geschickter's view[2] that there is a defect in development, whereby islets and strands of primitive cartilage persist throughout the

metaphysis. Their growth produces masses of cartilage which distort the architecture of the bone and tend to grow outward, projecting through defects in the overlying limiting periosteum, thereby producing external chondromas. The only argument against this theory is that the lesions have been reported in membranous bone[6] as well as in cartilaginous bone. Our case is an example of this, showing involvement of the iliums as well as the long bones.

Regardless of the histogenesis, chondrodysplasia is a disease of abnormal cartilaginous growth at the metaphysis of bones, in which the direction of growth of the cartilage may be directed either away from, or into the bone shaft, leading to expansion of the ends and profound alterations in their architecture[5]. When the growth is directed outward, external chondromas (exostosis, osteochondromas) are formed. If the growth is directed into the shaft, internal chondromas (enchondromas) develop. There is often a narrowing and irregularity in the epiphysial cartilages which tend to unite prematurely, producing dwarfing in the severe cases. Deformities may develop since there is often a difference in the degree of arrest of growth in the various long bones. Clubhand, knock knees, and valgus deformities of the foot are not uncommon[1].

The most striking feature of the disease is the bony outgrowths, which may be knob-like projections, spicules, or pedunculated masses. These usually produce little interference with joint motion since they tend to point away from the joint[3]. They may, however, be subject to trauma, or may cause pressure on nerves or vessels. Cases have been reported in which the lesions have undergone sarcomatous changes[2].

The disease is definitely hereditary in nature. Several previous reports showing involvement of three generations of a family have appeared in the literature. Venzant[5] describes a family in which 36 out of 78 members, over five generations, developed the characteristic bony changes. He feels that chondrodysplasia is a dominant hereditary trait.

Chondrodysplasia does not usually offer any great diagnostic difficulties, because of the typical lesions and the family history. Ollier's disease, which is probably a subvariety of chondrodysplasia, is characterized by multiple internal chondromas involving the shafts of tubular bones. These tend to be unilateral and cause marked deformity[3]. There is not usually a family history of similar bone deformities. Sometimes, internal chondromas are limited to the bones of the hands and feet[4]. Rickets, syphilis, the osteochondritides, and various rare bone conditions are quite easily differentiated.

No therapy is indicated in the usual case of chondrodysplasia since seldom does the disease cause any difficulties. If pressure on vessels or nerves develops and joints become limited in their motion, or if the over-

lying soft tissue is constantly being traumatized, surgical excision of the offending lesion is indicated[7]. Deformities, if they are severe enough to cause any incapacity, should be corrected by the usual orthopedic procedures. All patients should be examined once a year and should be warned to report a sudden increase in size of any of these lesions, since this will be the only clue to malignant change[3]. The ultimate elimination of this disease entity is a sociologic problem. In view of the evidence that chondrodysplasia is a dominant hereditary trait, people with the disease should be advised as to the probability of their children developing the same condition.

SUMMARY

A case of hereditary deforming chondrodysplasia is presented and the pertinent facts of the disease are discussed.

REFERENCES

1. Ehrenfried, A. H.: Hereditary Deforming Chondrodysplasia: A Review of the American Literature and a Report of Twelve Cases, J. A. M. A. **68**: 509, 1917.
2. Geshickter, C. F. and Copeland, M. M.: Tumors of Bone, 2nd ed. Am. J. Cancer, New York, 1936.
3. Coley, B. L.: *Neoplasms of Bone*, Paul B. Hoeber, Inc. New York.
4. Caffey, J.: *Pediatric X-ray Diagnosis*, 2nd Ed. The Yearbook Publishers, Chicago, 1950.
5. Vanzant, B. T.: Hereditary Deforming Chondrodysplasia, J. A. M. A. **119**: 786, 1942.
6. Mahorner, H. R.: Dyschondroplasia, J. Pediat. **10**: 1–26 (January) 1937.
7. Cohn, I.: Dyschondroplasia, Ann. Surg. **123**: 673, 1946.
8. Warkany, J.: In *Mitchell-Nelson Textbook of Pediatrics*, 5th Ed. W. B. Saunders Company, Philadelphia, 1949.
9. Todd, T. W.: *Atlas of Skeletal Maturation* (Hand), C. V. Mosby Co., St. Louis, Mo.